Clinical Trial Results of Topical Growth Factor Gel for Vaginal Atrophy Treatment

Clinical results of Cellese Growth Factor topical vaginal rejuvenation treatment, containing human growth factors. The results of the trial proved the efficacy of a home-care solution to improve symptoms of vaginal atrophy.

Abstract:

A four-week clinical study was conducted at the Urogynecology Unit Hospital Universitario in San Jorge Pereira, Colombia from April 2018 to June 2018.

To evaluate the effectiveness of a topical treatment for atrophic vaginitis, 10 post-menopausal female volunteers ranging in age from 53-66 participated in a four-week trial. All of the subjects exhibited Genitourinary symptoms related to Genitourinary Syndrome of Menopause (GSM) within the previous 24 months. Two gynecologists carried out the clinical evaluations. Volunteers received specially formulated growth factor gel in a nozzle crimp tube applicator.

The formulation was comprised of multiple human growth factors and hyaluronic acid. Sufficient product was provided to enable study subjects to use one tube every three days for the duration of the four-week study. Volunteers were instructed to apply the contents of the tube applicator into the vagina cavity and wall, discarding the empty tube following treatment.

During the four-week period, 8 of the 10 women completed the clinical trial. The symptoms used in the study to evaluate before and after results were: Dryness, itching, dyspareunia, pressure, dysuria, urgency, urinary tract infection, and stress incontinence. The results were calculated and averaged using a scale of zero to five, with zero being no symptoms, and five being severe symptoms.

At the end of the study, visual examination revealed dramatic changes in quality of vaginal mucosa, and vulvar and perineal skin. Histological studies showed recovery of vaginal tissue (epithelium and stroma) in the treated areas. Subjects reported marked improvement in dryness, itching, burning, dyspareunia, dysuria, urgency, incidence of urinary tract infections and stress incontinence.

Introduction:

Vaginal atrophy, also known as genitourinary syndrome of menopause (GSM), is attributed to the estrogen deficiency that occurs at the end of a woman's reproductive years. Although half of women develop GSM, only one in ten seeks treatment. Often related to a wide range of uro-gynecological symptoms, GMS involves the thickening of collagen fibrils and disorganization of total collagen content, mainly due to decreased collagen I synthesis and increased fibrilfragmentation.

The most common symptoms associated with vulvo-vaginal atrophy are dyspareunia, vaginal dryness, irritation, recurrent urinary tract infection, and urinary incontinence, which negatively affect the patient's quality of life and sexuality.

The homecare vaginal rejuvenation utilized is a non-hormonal and non-surgical rejuvenation topical product that appeared to be safe, effective, and a convenient treatment for vaginal atrophy.

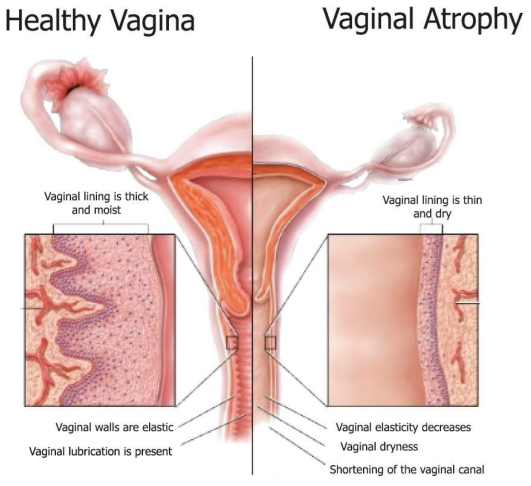
Current treatments such as systematic estrogen therapy, laser, topical estrogens, dilators, vaginal inserts, rings, and patches have undesired side effects, can be costly, and may cause discomfort during the treatment process.

Despite numerous treatment options, many perimenopausal and postmenopausal women continue to suffer symptoms of vaginal atrophy. Following the onset of vaginal atrophy, and without treatment, symptoms often increase as estrogen levels naturally decrease. The psychological aspect and sensitive nature of this condition can negatively impact one's emotional and physical well-being.

The proprietary bio-signal treatment consists of a box of six, 4ML disposable plastic crimp-tubes with attached insertion nozzles. (Each participant received two boxes for home use during the four-week study).

The product contains human stem cell-derived bio-signals and recombinant versions of KGF, KGF2 and VEGF growth factors, which support healing, promote epithelial cellular proliferation and mitigate inflammation.

Each ingredient has peer reviewed literature and documented proof of efficacy in improving vaginal atrophy conditions commonly caused by low estrogen and the natural aging process.



Method:

A four-week study was conducted of 10 post-menopausal female volunteers ranging in age from 53-66, with clinically evaluated vaginal atrophy symptoms.

- Difficult or painful sexual intercourse, (Dyspareunia).
- Vaginal dryness, irritation, and burning.
- Urinary symptoms including urgency, dysuria, nocturia, and urinary incontinence.
- Recurring urinary tract infections.

Two gynecologists enrolled five patients each for the purpose of testing a topical non-pharmaceutical an non-hormonal vaginal rejuvenation gel to restore a natural micro-environment, and to improve vaginal atrophy symptoms caused by low estrogen.

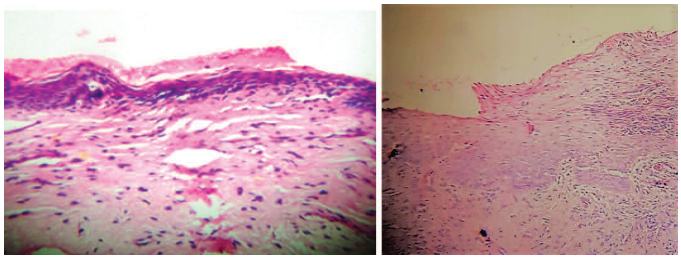
The volunteers provided written consent to participate and share before and after experiences. During the study, two subjects elected to end their participation.

Biopsies of the vagina were obtained before and after four-weeks of growth factor treatment. The vaginal samples were subjected to basic and special histological studies performed by blinded pathologist to identify trophic changes after treatment. The pathologist used both Hematoxylin and Eosin (H&E) and modified Masson's trichrome staining.

Each subject was provided with vaginal rejuvenation gel containing human stem cell-derived bio-signals and laboratory synthesized recombinant human growth factors. Sufficient product was provided to enable study subjects to use one tube every three days for the duration of the four-week study.

To administer the vaginal rejuvenation product, the female volunteers were instructed to hold the applicator tube at the wide-end, shake the product downward toward the narrow tip, and snap off the seal.

The tube was to be inserted and squeezed into the vaginal cavity, using the fingertip to target desired areas in and out of the vaginal region. The applicator tube was to be discarded after use.



Histological analysis of the vaginal mucosa by modified Masson's trichrome staining. Pre: Dense and disorganized collagen and atrophy (100x). Post: Epithelium with several layers of cells of stromal maturation with an increase in collagen (40x)

Results Summary:

A total of nine symptoms of vaginal atrophy were assessed over a four-week period.

Subjects who completed the four-week trial evaluated the convenience of the at-home, self-administered treatment, the ease of its application, as well as the physical and cosmetic results.

Important clinical and histological changes were seen during the four-week course of treatment.

Upon clinical examination at the end of the treatment period, the quality and trophism of both the vaginal mucosa and the vulvar skin, and perineal area showed dramatic improvement.

Primary Outcome

Clinical changes related to vaginal atrophy as evaluated by clinical examination, and changes in the VH1 and FSFI score.

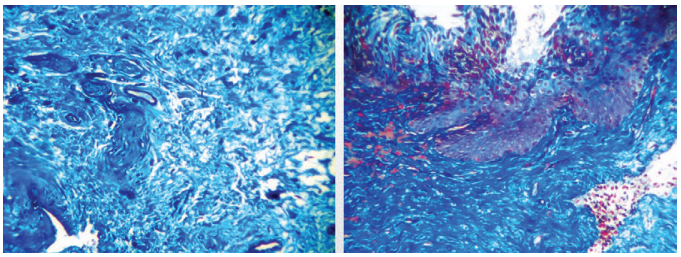
Secondary Outcomes

Cosmetic improvement of the vulvar and perineal area as evaluated by a Vulvar Symptoms Questionnaire (VSQ). Twelve treatment satisfaction as evaluated using a visual analogue scale (VAS) from the baseline conditions to the end of treatment.

All 10 subjects completed the protocol (Table I).

Table I
Demographic variables of the subjects (n=10)

Age (± SD) (years)	56.9 (± 3.19)
BMI (± SD) (kg/m2)	24.4 (± 1.55)
Parity (± SD)	2.5 (± 0.6)
Marital Status (%)	
Married	50.0
Single	50.0

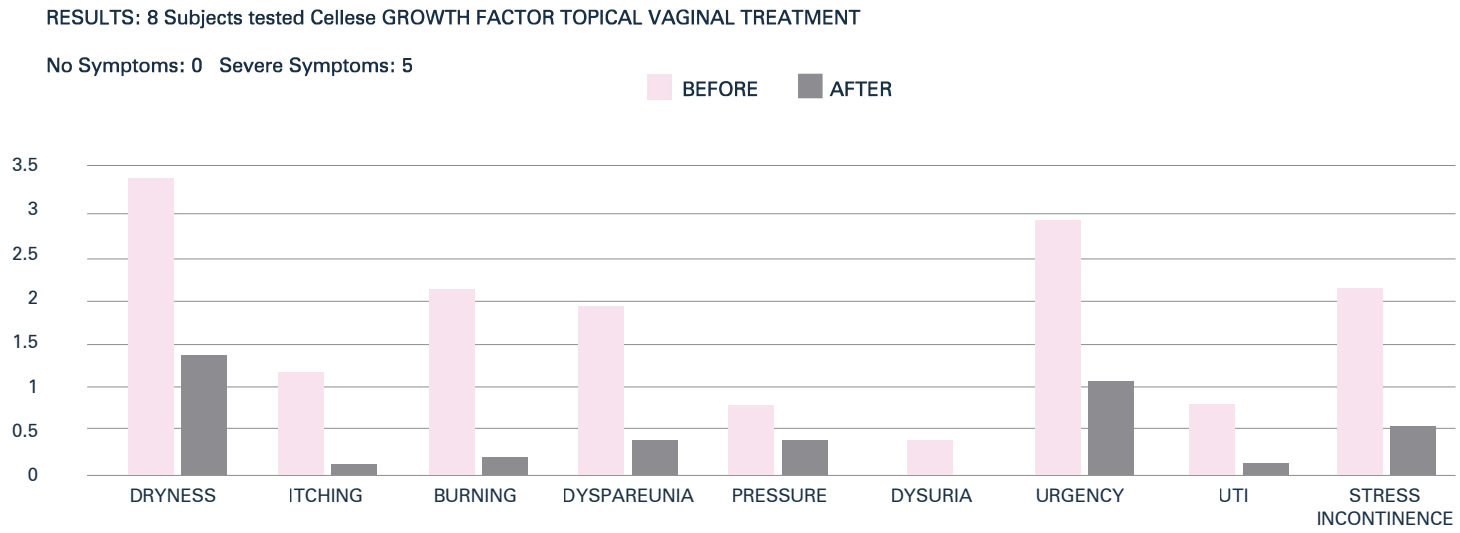


Histological analysis of the vaginal mucosa by Hematoxylin and Eosin staining. Pre: Flattened epithelium and atrophic stroma with dense small cells (100x). (Right) Post: Epithelium with extra cell layers, stroma growth, and more fibroblasts (40x).

Results Summary Cont.:

All of the subjects who were treated with topical growth factors showed improvements according to scores on the visual analogue scale (VAS) and vaginal health index (VHI).

All patients reported high levels of satisfaction with the results regarding symptoms related to GSM as well as cosmetic improvement in the labia majora and perineal area. No side effects were reported by any of the subjects.



Professional rating: Score of subjects showing improvements over 9 key categories

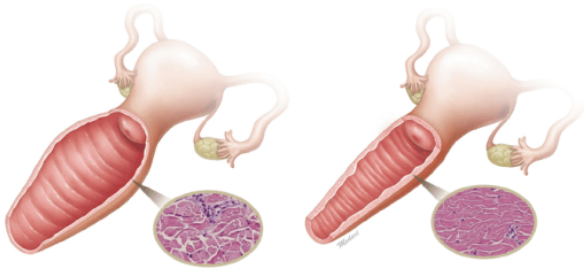
Discussion:

Topical Bio-Signals

The relationship between estrogen receptor activation and influence on downstream cytokine/growth factor cascades is well established.

As signaling proteins, growth factors work at the cell transcription level to up-regulate sex steroid receptors.
They can also induce cellular proliferation, differentiation, and apoptosis without the side effects sometimes reported by patients using topical estrogen therapy.

Hence, application of selective offer a non-hormonal option for peri and post-menopausal GSM.



(Before treatment) (After treatment)

Selected References:

Genitourinary syndrome of menopause: new terminology for vulvovaginal atrophy from the International Society for the Study of Women's Sexual Health and the North American Menopause Society. Menopause 2014;21:1063-8.

Vulvovaginal atrophy is strongly associated with female sexual dysfunction among sexually active postmenopausal women. Menopause 2008;15:661-6.

Genitourinary syndrome of menopause: an overview of clinical manifestations, pathophysiology , etiology , evaluation and management. Am J Obstet Gynecol 2016;215: 704-11.

Questionnaire: a questionnaire for measuring vulvovaginal symptoms in postmenopausal women. Menopause. 2013 Sep;20(9):973-9.

Topical KGF treatment as a therapeutic strategy for vaginal atrophy in a model of ovariectomized mice
Joun Cell Mol Med 2014 Sept

Keratinocyte growth factor injected into female mouse neonates stimulates uterine and vaginal epithelial growth. Endocrinology. 1998 Sept

Keratinocyte growth factor as a cytokine that mediates mesenchymal-epithelial interaction.
EXS. 1995

An overview on keratinocyte growth factor: from the molecular properties to clinical applications.
Protein & Peptide Letters 2014

Efficacy and safety of hyaluronic acid vaginal gel to ease vaginal dryness: a multicenter, randomized, controlled, open-label, parallel-group, clinical trial.
J Sex Med. Jun 2013

The effects of hyaluronic acid vaginal gel on the vaginal epithelium of ovariectomized rats.
Gynecol Endocrinol. 2015 Mar

Efficacy of a medical device containing liposomal hyaluronic acid against vulvovaginal dryness Gynecol Obstet Fertil. 2015 Jun

Is vaginal hyaluronic acid as effective as vaginal estriol for vaginal dryness relief?
Gynecol Obstet. 2013 Dec;288(6)

Don't ignore vaginal dryness and pain. The condition is treatable, although treatments likely won't provide complete relief.
Harvard Women's Health Watch 2019 Mar